Seroprevalence and hematological profile of dengue among healthy inhabitants of Mayo Kebbi province: South of Tchad

Mahamat Baharadine Djibrine[1,2], Ngum Lesley Ngum[1,3,4], Boda Maurice[2], Jean Paul Kengne Chedjou[5], Palmer Masumbe Netongo[1,6]

[1]Molecular Diagnostics Research Group, Biotechnology Center, University of Yaoundé 1, Cameroon, [2]Department of Microbiology, Faculty of Science, University of Yaoundé 1, Cameroon, [3]Department of Biochemistry, Faculty of Medicine and Biomedical Science, University of Yaoundé 1, Cameroon, [4]Institute of Medicine and Medicinal Plants Studies, IMPM, Yaoundé, Cameroon, [5]Department of Biochemistry, Faculty of Science, University of Buea, Cameroon, [6]Department of Biochemistry, Faculty of Science, University of Yaoundé 1, Cameroon

ABSTRACT

Introduction: Dengue is one of the most serious and rapidly spreading major mosquito borne diseases in the world. Despite many acute febrile illnesses in Tchad, the burden of illness due to dengue in the country is largely unknown. Hence, the present study aimed to determine the seroprevalence of dengue viral (DENV) infection and its association with hematological parameters. **Method:** A cross sectional study was carried out in Bongor Provincial Hospital. Blood samples were collected from each participant and were used to determine the hematological profile and to diagnose the presence of DENV infection. A total of 130 participants were enrolled in the study. Among these, 114 (87.7%) were diagnosed positive for DENV infection. **Results:** The majority of the positive cases were of the age group 21 to 40 years old. Leukocytosis was the most common hematological parameter affecting 120 (92.3%) of them followed by anemia and thrombocytopenia affecting 69 (53.1%) and 16 (12.3%) of them, respectively, and then lymphocytosis affecting 5 (3.8%) of them. No case of leukopenia was recorded. **Discussion:** The seroprevalence rate among participants suggests that the dengue virus is in circulation in Mayo Kebbi province: south of Tchad. The abnormal hematological parameters may contribute to the severity of the infection like the incidence of bleeding in the case of thrombocytopenia.

Keywords: Dengue, hematological profile, leukopenia, seroprevalence, thrombocytopenia

Introduction

Dengue viral (DENV) infection is one of the major mosquito-borne diseases caused by dengue virus belonging to Flaviviridae. Dengue is a viral disease transmitted by mosquitoes of the genus Aedes.[1,2] Almost half of the world's population,

about 4 billion people, live in areas with a risk of dengue. The incidence of dengue has markedly increased over the past two decades worldwide with 129 countries affected by this substantial public health challenge.[3-5] This acute self-limiting systemic febrile illness can be caused by any of the four non-segmented, single-stranded, positive-sense, enveloped RNA serotypes (DENV-1, DENV-2, DENV-3, and DENV-4). So, a person has a chance to be infected four times in his life, as infection with one serotype of DENV provides lifelong immunity to the specific serotype. Genetically, dengue serotypes are closely

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related to each other but they are anti-genetically distinct from each other.[6,7] Dengue disease severity varies from asymptomatic infection to a variety of illnesses ranging from an influenza-like self-limiting illness to a potentially lethal disease such as dengue hemorrhagic fever (DHF) or dengue shock syndrome (DSS).[8] It is a complex disease with various clinical presentations, which often go unrecognized or misdiagnosed as other common fever-causing tropical diseases.[9] DENV infection causes flu-like illness that can develop into a severe complication and even death in children as well as in adults.[2] The DENV mosquito vector is endemic to tropical and sub-tropical climates but with a recent unprecedented worldwide geographical expansion.[10,11] However, transfusion transmission, air travel, and global warming firmly establish DENV as an emerging threat to healthcare systems worldwide, expanding the risk far outside the equatorial zone.[2,12] Globally, there are approximately 390 million DENV infections reported each year with over 2% resulting in a fatal outcome. Dengue outbreaks persistently challenge regional health systems and the economy, particularly in developing countries where they are more prevalent.[13,14] Furthermore, diagnosing patients with acute dengue is challenging due to the similarity of clinical symptoms during early illness and the poor sensitivity and specificity of point-of-care diagnostic tests. While vaccines and mosquito control methods are welcome, they alone are unlikely to fully reduce the burden of dengue, and treatment for dengue is therefore essential.[15] DENV infection is endemic in more than 100 countries across the Americas, East Mediterranean, Western Pacific, Africa, South-East Asia, and Europe.[16] In Africa, dengue has been reported in 34 countries, mostly in Eastern Africa.[17] Dengue has been frequently detected in travelers returning from over 30 African countries. Dengue is highly prevalent in central Africa with cases reported in Cameroon and Gabon.[2,18,19] To the best of our knowledge, there is relatively no available data for the seroprevalence of dengue in Chad, that is, the frequency of individuals in Chad with dengue antibodies in their blood serum.

Infection with dengue can be diagnosed by using clinical presentations and laboratory tests.[20] The most prominent hematological changes are thrombocytopenia and leukopenia. Lymphocytosis is commonly noted with reactive lymphocytes. During the progression of dengue fever, a progressive increase in hematocrit concentration of almost up to 20% increase from the patient's baseline is usually observed.[10,11] DHF and/or DSS are the major cause of mortality lead by multiple reasons for abnormal hemostasis, thrombopathy, and coagulation derangements.[14,21] Hence, with this view, the present study was designed to evaluate the seroprevalence of dengue and its association with hematological profiles among healthy inhabitants in Mayo Kebbi province: south of Chad.

Method

Study site

Mayo Kebbi is one of the province in Tchad with Bongor as capital. Mayo Kebbi is situated southwest of the country and shares a boundary with Cameroon. It is located at latitude: 9° 17' 60.00" N and at longitude 13° 32' 59.99" E. It has about 769178 inhabitants on an 18 186 km² surface area. The population density of Mayo Kebbi is 42,3 inhabitants per km². The climate here is dry and semi-arid with agriculture and fishing being the main activities of the inhabitants.[22]

Ethical consideration

Participation in the study was voluntary, with informed consent obtained from each participant. Detailed information regarding the study objectives and procedures was explained to all the participants before collecting any data or samples. Only participants who agreed verbally and signed a written informed consent were allowed to take part in the study. A signed assent form was also obtained from children who were neither considered minors or adults whose parents/guardians consented. Children who were considered minors were included in the study only after a signed consent from their parent/guardian. Blood samples were collected by an experienced laboratory technologist. Participants had full right to continue or withdraw from the study. The confidentiality of all participants was maintained throughout the study. At the time of the study, owing to the political situation in Chad, the ethical committee board was not functional but authorization to conduct the study was given by the Provincial delegation for health in collaboration with the director of the Bongor Provincial Hospital.

Study design and participants

A non-randomized cross-sectional hospital-based study was carried out. Participants were recruited by convenience sampling technique. The study was conducted among febrile patients who were presumed for dengue infection based on 2009 WHO criteria[23] and seeking routine medical care at the inpatient and outpatient department of Bongor Provincial Hospital from September 2019 to February 2022.

Sampling

Participants who met the inclusion criteria were screened by a physician. Demographic variables, clinical features, and awareness of DENV infection were collected by a nurse using a structured questionnaire. About 5 mL of blood sample was collected into a sterile ethylenediamine tetra-acetic acid (EDTA) tube from each participant by venipuncture. About 2 mL of the blood was used to determine the hematological parameters. The remaining blood sample was then centrifuged at 3000 × g for 5 min. Micropipette was used to aliquot serum into sterile 1.5 mL Eppendorf tubes and were stored at -20°C for subsequent analysis.[24]

Determination of hematological parameters

The hematological parameter was done with 2 mL of venous blood samples on an EDTA tube labeled with participant information. The blood sample was examined for hemoglobin count, hematocrit, white blood cell (WBC) count, platelet count, and lymphocyte count. An automated cell counter analyzer Mindray BC3000 (Mindray Nanshen Schenzhen 518057, PR, China) was used to analyze the blood in accordance with the manufacturer's instructions.

Detection of dengue virus using ELISA

Sera samples were removed from -20°C, brought to room temperature, and assessed for anti-dengue IgG using enzyme-linked immunosorbent assay (ELISA) (DIA source Immunoassays S.A, Belgium) The overall seroprevalence of DENV infection in this study was higher than findings in Ethiopia 33.3% Getachew F, *et al.*,[27] 56.8%,[28] in Eritrea 33.3%,[29] in Tanzania 7.7%,[30] in Kenya, 12.5%[31] and in Thailand, 51.5%.[32] This difference in prevalence may be because some of the studies used both ELISA and polymerase chain reaction (PCR) to check for DENV infection whereas we only used ELISA.

Statistical analysis

Statistical analysis was performed with a statistical package for social sciences (SPSS) software (version 22.1). The mean, frequencies, and percentages were used to summarize descriptive statistics of the data. The Chi-square ($x2$) test was used to assess associations between variables.

Results

Demography and characteristics of study populations

A total of 130 participants were enrolled in the study aged from 8 to 80 (mean age; 29.3 ± 1.07). The majority of the patients were of the 21–40 years age group (n = 86, 66.2%). The majority of the participants were male (n = 75, 57.7%) as compared to their female counterparts (n = 55, 42.3%). All 130 participated and completed the questionnaire. When the participants were assessed for their knowledge of DEVI, only 22 (16.9%) of them confirmed having heard or being aware of dengue virus infection, and the remaining majority about 108 (83.1%) confirmed to know nothing about dengue virus. Regarding the participants distribution in terms of their occupation, the majority of the participants were students numbering 77 (59.2%), followed by housewives, farmers, business owners, and employees each numbering 19 (14.6%), 16 (12.3%), 11 (8.5%), and 7 (5.4%). Regarding marital status, most of the participants were single about 80 (61.5%) with 5 (3.8%) either widows or divorcees. The remaining 45 (34.6%) were all married men and women as shown in Table 1.

All the 130 participants were assessed for seroprevalence of dengue. Of the 130 participants, 114 were DENV seropositive, giving a seroprevalence rate of 87.9%. The majority of those positive for DENV infection were of the 21–40 years age group, with 79 of the 86 participants within this age group diagnosed positive for DENV infection, giving an age group seroprevalence rate of 91.9%. This was closely followed by the 5–20 age group with 20 of the 29 participants within this age group diagnosed positive for DENV infection and finally the 40–80 age group with all 15 participants diagnosed positive for DENV infection. Of the 114 DENV-positive diagnosed participants, 66 of them were men with a seroprevalence rate of 88.0% among the male participants. The number of female participants diagnosed positive for DENV infection stood at 48 with a seroprevalence rate of 87.3% within the female participants as shown in Table 1.

All 130 samples collected from participants were assessed for hematological profile and their association with DENV infection seroprevalence was determined. WBC count, platelet count, hematocrit count as well as their proportion among participants was documented [Figure 1]. When the WBC count was determined, the majority of the participants about 120 (92.3%) had leukocytosis (WBC >11 × 10⁹/L) among which 108 (94.7%) were positive for DENV. No case of leukopenia was observed [Table 2] and (wbc <4 × 10⁹/L) was observed. Lymphocytosis (lymphocyte level >4.5 × 10⁹/L) was observed in 28 (21.5%) participants among which 24 (21.1%) were positive for DENV. Lymphocytosis (lymphocyte level <1 × 10⁹/L) was observed in five (3.8%) of the participants with four (3.5%) diagnosed positive for DENV infection. Anemia (hemoglobin level <12 g/dL) was observed in 69 (53.1%) participants. Participants were also assessed for thrombocytopenia (platelet level <150 × 10⁹/L). Of the 130 participants assessed, thrombocytopenia was observed in 16 (12.3%), 13 (11.4%) of which were positive for DENV infection. Hematocrit level was also determined; the majority of the participants about 83 (63.9%) had abnormal hematocrit concentrations, among which 76 (58.5%) had a hematocrit level <35.5% and 7 (5.4%) had a hematocrit level > 48.6.

Discussion

Limitations of current available dengue prevention and control strategies like vaccines, effective vector control measures as well as poor knowledge existing on it are responsible for the dramatic increase in the global prevalence of dengue. Also, the non-availability of treatment for dengue makes it a threat to primary healthcare especially in the tropics.[16,25,26] Owing to the insufficient DENV infection-related information in Tchad and the absence of this information in Mayo Kebbi province, this study therefore aimed at determining the seroprevalence of DENV infection and their association with hematological profiles of Mayo Kebbi province inhabitants: south of Tchad. In this study, 130 Mayo Kebbi inhabitants were assessed for DENV infection, out of which 55 (42.3%) were females and 75 (57.7%) males. The overall seroprevalence of DENV infection in the present study stood at 114 with a seroprevalence rate of 87.7%. Among this positive case, 48 (87.3%) were females, and 66 (88.0%) were males. When the seroprevalence was compared among different age groups, a significant (pv = 0.002) distribution of DENV infection was observed, with an increasing seroprevalence observed in the 5–20 (69.0%) years age group to the 40–80 (100.0%) years age group. No statistical significance was observed when DENV infection seroprevalence rate was compared with gender (pv = 0.974), marital status (pv = 0.883), knowledge (pv = 0.735), and occupation (pv = 0.973). Also, in this study, more men were reported to be positive for DENV infection. To contribute to the enhancement of primary healthcare, the hematological profiles of all the participants were

| Table 1: Socio-demographic characteristics and seroprevalence status of participants (n=130)					
Characteristics	**No. (%)**	**Negative (%) (N=16)**	**Positive (%) (N=144)**	**X²**	**Pv**
Age				17.248	0.002
5-20	29 (22.3)	9 (31.0)	20 (69.0)		
21-40	86 (66.2)	7 (8.1)	79 (91.1)		
40-80	15 (11.5)	0 (00.0)	15 (100.0)		
Total	130	16 (12.3)	114 (87.7)		
Gender				0.052	0.974
Female	55 (42.3)	7 (12.7)	48 (87.3)		
Male	75 (57.7)	9 (12.0)	66 (88.0)		
Marital status				2.371	0.883
Divorced/widowed	5 (3.8)	0 (00.0)	5 (100.0)		
Married	45 (34.6)	4 (8.9)	41 (91.1)		
Single	80 (61.5)	12 (15.0)	68 (85.0)		
Knowledge				0.615	0.735
Yes	22 (16.9)	3 (13.6)	19 (86.2)		
No	108 (83,1)	13 (12.0)	95 (88.0)		
Occupation				2.222	0.973
Student	77 (59.2)	9 (11.7)	68 (88.3)		
Employed	7 (5.4)	1 (14.3)	6 (85.7)		
Business	11 (8.5)	1 (9.1)	10 (90.9)		
Housewife	19 (14.6)	3 (15.8)	16 (84.2)		
Farmer	16 (12.3)	2 (12.5)	14 (87.5)		
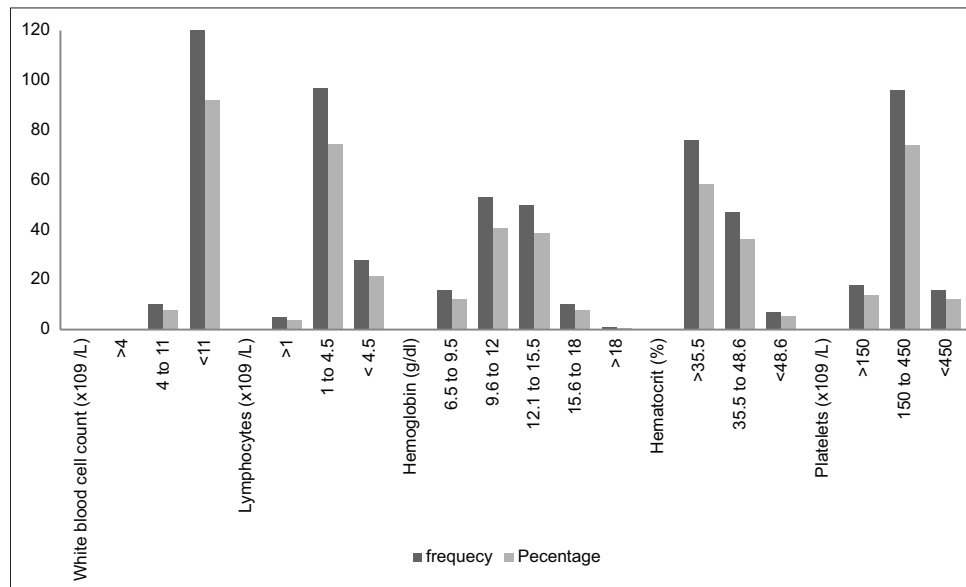
Figure 1: Proportion of participants' hematological profiles

determined. These profiles were regrouped into classes, which permitted us to easily conclude which of the parameters were either over- or under-expressed. The hemoglobin levels ranged from 8.6 to 18.9 g/dL with hematocrit levels ranging from 18% to 47.7%. In our study, participants had WBC count ranging from 5000 to 127000/mm³. The lymphocyte count ranged from 7000 to 85000/mm³.

The overall seroprevalence of DENV infection in this study was higher than findings in Ethiopia 33.3% Ferede Getachew *et al.*,[27] 56.8%,[28] in Eritrea 33.3%,[29] in Tanzania 7.7%,[30] in Kenya, 12.5%[31] and in Thailand, 51.5%.[32] This difference

in prevalence may be because some of the studies used both ELISA and polymerase chain reaction (PCR) to check for DENV infection whereas we only used ELISA. It may also be due to differences in environmental factors such as rainfall, temperature, and humidity which are critical factors for the transmission of dengue.[2,3] This prevalence was similar to that obtained by Dhanoa A, *et al.* in southern Malaysia where they obtained a prevalence of 86.6%.[11] A similar trend in age group distribution was observed in a study in southern Malaysia with a 95% seroprevalence rate in the older participants.[11] This can be justified by the fact that as one gets older in a dengue-endemic area, he or she is repeatedly exposed to the DENV infection

Parameters	Frequency (%)	ELISA		X^2	PV
		Positive (%)	Negative (%)		
White blood cell count (×10^9/L)				9.709	0.008
>4	00 (0.0)	00 (0.0)	00 (0.0)		
4-11	10 (7.7)	6 (5.3)	4 (25.0)		
<11	120 (92.3)	108 (94.7)	12 (75.0)		
Lymphocytes (×10^9/L)				1.654	0.799
<1	5 (3.8)	4 (3.5)	1 (6.2)		
1-4.5	97 (74.6)	86 (75.4)	11 (68.8)		
>4.5	28 (21.5)	24 (21.1)	4 (25)		
Hemoglobin (g/dL)				8.254	0.409
6.5-9.5	16 (12.3)	13 (11.4)	3 (18.8)		
9.6-12	53 (40.8)	48 (42.1)	5 (13.2)		
12.1-15.5	50 (38.5)	43 (37.7)	7 (43.8)		
15.6-18	10 (7.7)	9 (7.9)	1 (6.2)		
>18	1 (0.7)	1 (0.9)	0 (0.0)		
Hematocrit (%)				1.794	0.774
>35.5	76 (58.5)	63 (56.3)	11 (68.8)		
35.5-48.6	47 (36.2)	42 (37.5)	5 (31.2)		
<48.6	7 (5.4)	7 (6.3)	0 (0.0)		
Platelets (×10^9/L)				1.916	0.751
>150	18 (13.8)	16 (14.0)	2 (12.4)		
150-450	96 (73.8)	85 (74.6)	11 (68.8)		
<450	16 (12.3)	13 (11.4)	3 (18.8)		

Table 2: Hematological profiles of study participants and their association with DENV infection seroprevalences

Key; L=liters, g=grams, dL=deciliters

through its vector. There was a difference in the proportion of men with DENV compared to other studies where rather more DENV infections were reported from women.[14] However, many studies have reported a higher prevalence of DENV infection in men as compared to women.[33-35] Similar findings of hematological profiles were observed by Supriya Karmakar *et al.*[36] and Kailash C Meena *et al.*[37] This range in WBC was however different from (4000–11000/mm^3) observed by Supriya Karmakar *et al.*[36] In the case of the WBCs, no count was observed on the lower side of the normal limit; this however differed from results reported by others where counts were recorded within the lower normal limit.[37-39] Among the hematological profiles, leukocytosis was the most common finding. This however differs from other similar studies where thrombocytopenia was reported to be the most common hematological parameter.[27,40] The leukocytosis may be due to an increase in the production of leukocytes due to the presence of DENV infection in seropositive participants. Then, in participants who were negative for DENV infection, the high leukocyte levels may be justified by the fact that they have been harboring another infection like malaria, for instance, given that the study area is endemic to infectious diseases. No case of leukopenia was observed in our study whereas in other studies elsewhere leukopenia was observed in 26.5%[27] and 56.9%.[41] This implies that there was no bone marrow suppression among the DENV-infected seroprevalence participants.[42] Thrombocytopenia was observed in 12.3% of the participants. This differs from the 3.3% reported in another study. Thrombocytopenia might be due to decreased production of platelets due to suppression of the bone marrow by a virus and also due to the binding of dengue antigens to platelets and

increased antibody-mediated immunological destruction of platelets.[20,42] Hemoglobin levels less than the normal values were observed in 69 (53.1%) of the participants. This finding is consistent with another study.[43] Increased hematocrit was observed in seven (5.4%) of the participants in our study while it is less than the observation of the other studies which reported a 50%[44] and 27%[42] rise in hematocrit value; this great difference can be explained by the fact that we were working with asymptomatic participants but they worked with already confirmed DENV infected cases. A statistical significance was observed between WBC count (pv = 0.008), hemoglobin (pv = 0.409), and the DENV infection seroprevalence.

Conclusion

We reported a high incidence of dengue virus infection in the study area. Future large-scale investigations and molecular detection will be necessary to discover viral serotypes. The seroprevalence rate among participants suggests that the dengue virus is in circulation in Mayo Kebbi province: south of Tchad. The abnormality in some of the hematological parameters may contribute to the severity of the infection and may be a possible dengue outbreak.

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Conflicts of interest

There are no conflicts of interest.

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